Infrared and Raman Spectroscopy for Real-Time Inline Monitoring

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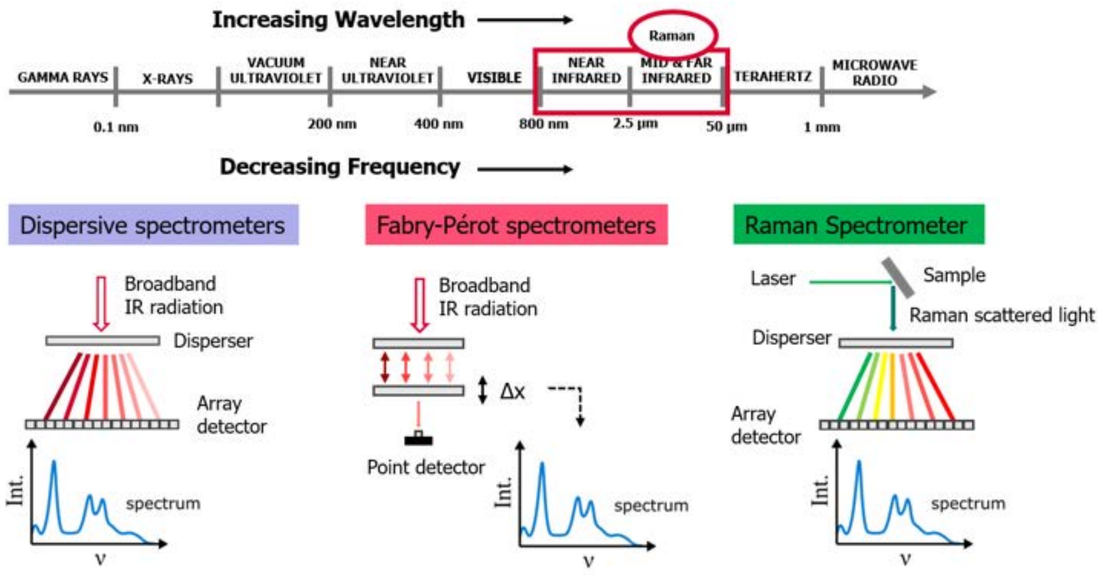
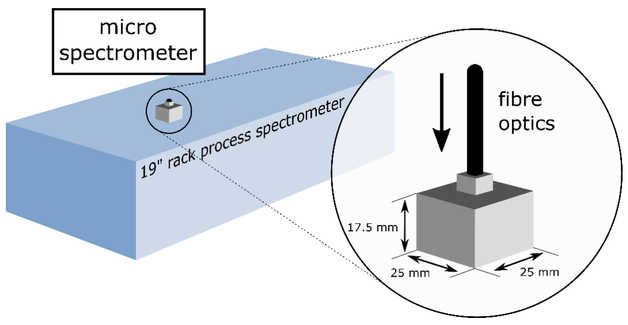
Infrared and Raman spectroscopy

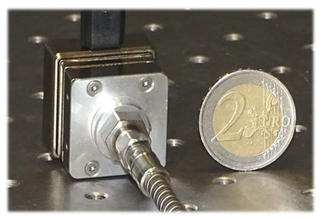


Schematics of different typically used spectrometer types

Evolution of spectrometers:
Technological advances enabled miniaturization of Infrared and Raman spectrometers. Costs cut by a factor of ~10 → < 3k€

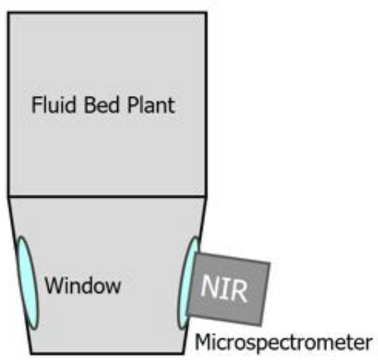
- Higher cost efficiency / lower price
- More compact hardware
- Higher ruggedness / less maintenance





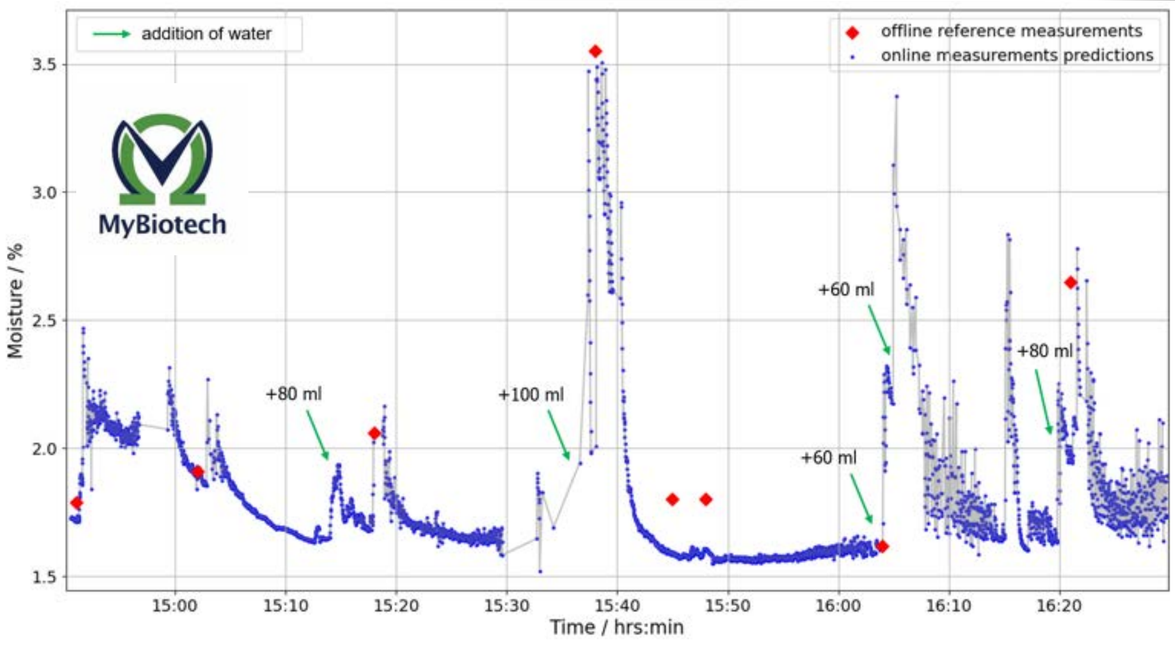
Near-infrared inline measurements

Moisture content in nanoparticles: inline measurements in a fluid bed pilot plant. Test measurements with Metolose SM 1500 in a fluid bed pilot plant; reference measurements were taken with Halogen Moisture Analyzer HC103/01 (Mettler Toledo);



- Continuous recording of Near-Infrared (NIR) spectra
- Evaluation of each spectrum by means of **multivariate data analysis**
- Calibration of model to **predict moisture content**
- Application of the model to the measured spectra

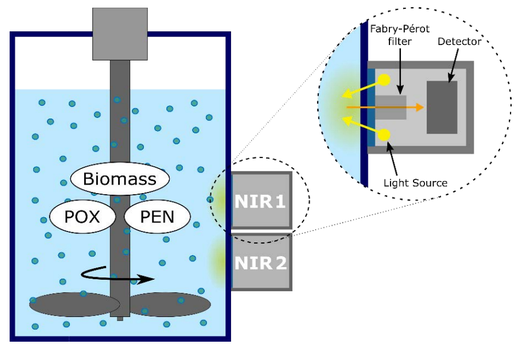
Schematics of the experiment; the near-infrared microspectrometer was attached to the viewing window



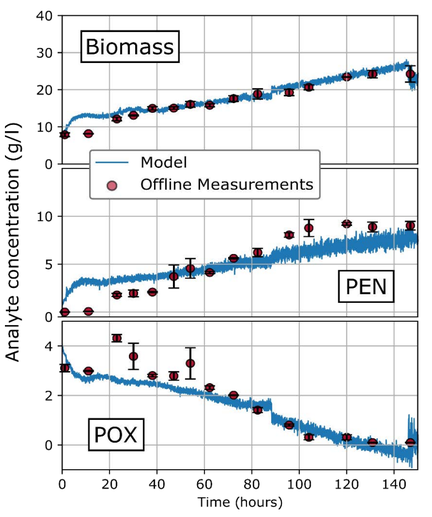
Inline moisture measurements of Metolose SM 1500 in a fluid bed pilot plant
Note: discrepancies due to inhomogeneity of the sampled material (sample agglomeration)

Bioprocess monitoring:
Near-Infrared monitoring of a *Penicillinum chrysogenum* fed-batch fermentation process through a glass window. Concentrations of biomass, Penicillin (PEN) and phenoxyacetic acid (POX) were tracked; partial least squares (PLS) regression models were established based on offline reference analytics [1];

- Results suggest a **significant potential** for **real-time**, **non-invasive NIR bioprocess monitoring**. This could help to **optimize both the yield and quality** of different biochemical products in the future



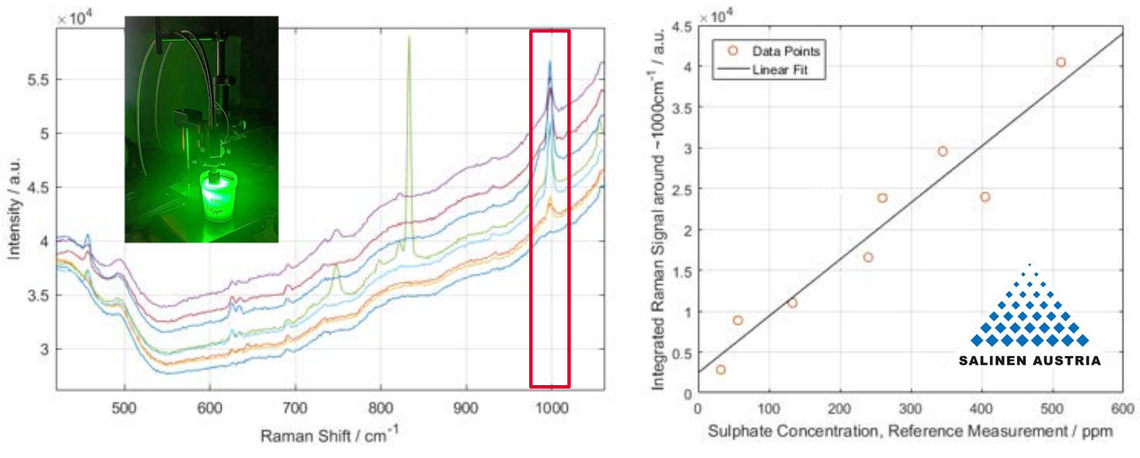
Top: schematics of the experimental setup; left: PLS-Model predictions for the three monitored analytes in the validation batch (blue line); reference values with respective error bars (red dots)



Raman inline measurements

Raman measurement of sulphate in salt:

- Preliminary laboratory measurements of salt samples with different sulphate concentrations
- Goal is to determine salt quality inline (high purity salt to be sold as pharmaceutical salt)
- One sample had high sodium-nitride content, which can nicely be measured simultaneously to the sulphate band
- Next step is to incorporate the method as inline measurement
- Potential reduction of costly reference measurements using Inductively Coupled Plasma (ICP) spectroscopy



Left: Raman spectra of salt samples; the sulphate peak is indicated in the red box around 1000 cm^{-1}; sodium-nitride can be seen around 830 cm^{-1}; Right: integrated Raman signal versus sulphate concentration; linear regression suggests limit of detection at 60 ppm;

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